

1. A nucleic acid encoding a polypeptide of between 150 and 299 amino acids that has an amino acid sequence at least 50% identical to that of the corresponding region of amino acids 1 to 299 of a mature, native human apoE polypeptide and that, when administered to or expressed in a mammal, lowers the total serum cholesterol level without inducing hypertriglyceridemia.

2. The nucleic acid of claim 1, encoding a polypeptide that has an amino acid sequence at least 80% identical to the corresponding region of a mature, native human apoE.

3. The nucleic acid of claim 2, encoding a polypeptide that has an amino acid sequence 100% identical to the corresponding region of a mature, native, human apoE.

4. The nucleic acid of claim 1, wherein the amino acid sequence of said encoded polypeptide is at least 80% identical to the corresponding region of a mature, native human apoE polypeptide, beginning at amino acid residue 1.

5. The nucleic acid of claim 1, wherein said encoded polypeptide has a signal peptide operably linked to said region of said mature apoE.

6. The nucleic acid of claim 1, wherein said encoded polypeptide consists of between 150 and 215 amino acids.

7. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 203 amino acids.

8. The nucleic acid of claim 1, encoding residues 1-203 of an apoE preprotein of any one of SEQ ID Nos. 14-19.

9. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 220 amino acids.

5 10. The nucleic acid of claim 1, encoding residues 1-220 of an apoE preprotein of any one of SEQ ID Nos. 14-19.

11. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 247 amino acids.

10 12. The nucleic acid of claim 1, encoding residues 1-247 of an apoE preprotein of any one of SEQ ID Nos. 14-19.

13. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 277 amino acids.

15 14. The nucleic acid of claim 1, encoding residues 1-277 of an apoE preprotein of any one of SEQ ID Nos. 14-19.

15. A polypeptide of between 150 and 299 amino acids, said polypeptide having an amino acid sequence at least 50% identical to the corresponding region of amino acids 1-299 of a mature, native, human apoE, said polypeptide, when administered to or expressed in a mammal, being capable of lowering the total
20 serum cholesterol level without inducing hypertriglyceridemia.

16. The polypeptide of claim 15, having an amino acid sequence at least 80% identical to the corresponding region of a mature, native, human apoE.

17. The polypeptide of claim 16, having an amino acid sequence 100% identical to the corresponding region of a mature, native, human apoE.

18. The polypeptide of claim 15, having an amino acid sequence at least 80% identical to the corresponding region of a mature, native, human apoE polypeptide, beginning at amino acid residue 1.

19. The polypeptide of claim 15, consisting of between 150 and 215 amino acids.

20. The polypeptide of claim 15, having an amino acid sequence identical to amino acids 1-185 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.

21. The polypeptide of claim 15, having an amino acid sequence identical to amino acids 1-202 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.

22. The polypeptide of claim 15, having an amino acid sequence identical to amino acids 1-229 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.

23. The polypeptide of claim 15, having an amino acid sequence identical to amino acids 1-259 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.

24. A method of lowering cholesterol, delaying the onset of atherosclerosis, or treating atherosclerosis in a mammal without inducing hypertriglyceridemia, said method comprising administering to said mammal a polypeptide of between 150 and 299 amino acids, said polypeptide having an amino acid sequence at least 80% identical to the corresponding region of amino acids 1-299 of a mature, native, human apoE, said polypeptide, when administered to or expressed in a mammal, being capable of lowering the total serum cholesterol level without inducing hypertriglyceridemia.

25. The method of claim 24, wherein said mammal lacks an endogenous, normally functioning apoE gene.

26. The method of claim 24, wherein said mammal is at risk for developing atherosclerosis due to accumulation of lipoprotein remnants in the bloodstream.

27. The method of claim 26, wherein said mammal has a defect in remnant removal.

28. The method of claim 24, wherein said mammal lacks an endogenous, normally functioning LDL receptor.

29. The method of claim 24, wherein said polypeptide is administered intramuscularly, intravenously, or subcutaneously to said mammal.

30. A method of lowering cholesterol, delaying the onset of atherosclerosis, or regressing atherosclerosis in a mammal without inducing hypertriglyceridemia, said method comprising administering to or expressing in said mammal a nucleic acid encoding a polypeptide of between 150 and 299

amino acids that has an amino acid sequence at least 80% identical to that of the corresponding region of amino acids 1 to 299 of a mature, native, human apoE polypeptide and that, when administered to or expressed in a mammal, lowers the total serum cholesterol level without inducing hypertriglyceridemia.

5 31. The method of claim 30, wherein said nucleic acid is operably linked to a promoter and contained in an expression vector.

32. The method of claim 30, wherein said nucleic acid is intravenously administered to said mammal in combination with a liposome and protamine.

10 33. The method of claim 30, wherein said nucleic acid is contained in a recombinant viral vector.

34. The method of claim 33, wherein said vector is administered intravenously.

35. The method of claim 33, wherein said vector is administered by bone marrow transplantation.

15 36. The method of claim 33, wherein said vector is administered to an artery at the site of a lesion.

37. The method of claim 33, wherein said vector is an adenoviral vector.

38. The method of claim 33, wherein said vector is an adeno-associated viral vector.

39. The method of claim 33, wherein said vector is a lentiviral vector.

40. The method of claim 33, wherein said vector is a herpes viral vector.

41. The method of claim 33, wherein said vector is a retroviral vector.

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42. The method of claim 33, wherein said vector is a baculoviral vector.

43. The method of claim 30, wherein said mammal lacks an endogenous, normally functioning apoE gene.

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44. The method of claim 30, wherein said mammal is at risk for developing atherosclerosis due to accumulation of lipoprotein remnants in the bloodstream.

45. The method of claim 40, wherein said mammal has a defect in remnant removal.

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46. The method of claim 30, wherein said mammal lacks an endogenous, normally functioning LDL receptor.

47. The method claim of 30, wherein said nucleic acid is administered to or expressed in the liver of said mammal.

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48. A pharmaceutical composition comprising a polypeptide admixed with a pharmaceutically acceptable carrier substance, said polypeptide consisting of between 150 and 299 amino acids and having an amino acid sequence at least 80% identical to the corresponding region of amino acids 1-299 of a mature, native, human apoE, said polypeptide, when administered to or expressed in a mammal,

being capable of lowering the total serum cholesterol level without inducing hypertriglyceridemia.

49. A recombinant DNA molecule comprising a nucleic acid operatively linked to a promoter, said nucleic acid encoding a polypeptide of between 150 and 299 amino acids that has an amino acid sequence at least 80% identical to that of the corresponding region of amino acids 1 to 299 of a mature, native, human apoE polypeptide and that, when administered to or expressed in a mammal, lowers the total serum cholesterol level without inducing hypertriglyceridemia.